NDA 21-061/S-005, S-006
NDA 21-062/S-006, S-007

Bristol Myers-Squibb Company
Attention: Joan Fung-Tomc, Ph.D.
Director, Regulatory Science
5 Research Parkway
P. O. Box 5100
Wallingford, CT 06492-7660

20 AUG 2001

Dear Dr. Fung-Tomc:

Please refer to your supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tequin® (gatifloxacin) Tablets, 200 mg and 400 mg as follows:

NDA 21-061 (Tablets)

SLR	Date submitted	Date received
005	October 5, 2000	October 6, 2000
006	December 13, 2000	December 14, 2000

Please refer to your supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tequin® (gatifloxacin) Injection, 200 mg and 400 mg as follows:

NDA 21-062 (Injection)

SLR	Date submitted	Date received
006	October 5, 2000	October 6, 2000
007	December 13, 2000	December 14, 2000

We acknowledge receipt of your submissions to both Tequin NDAs dated December 19, 2000 and April 17, 2001.

These "Changes Being Effected in 30 days" supplemental new drug applications provide for the following changes to the Tequin® label. The deleted text is noted by ~~strikethrough~~ and the added text is noted by double underline as follows:

1. CLINICAL PHARMACOLOGY

· In the **Glucose Homeostasis** subsection, the following paragraph was added and now appears first in this subsection:

"As with other quinolones, clinical experience has shown that disturbances of blood glucose, including symptomatic hyper- and hypoglycemia, have been reported in patients treated concomitantly with TEQUIN and oral hypoglycemic agents with or without insulin. Therefore, careful monitoring of blood glucose is recommended when TEQUIN is administered to diabetic patients receiving treatment with oral hypoglycemic agents with or without insulin. (See **PRECAUTIONS: General, Information for Patients,** and **Drug Interactions**.)"

· In the **Drug/Drug Interactions** subsection, a reference **(**See **PRECAUTIONS: General** and **Drug Interactions)** was added to the **Glyburide** statement.

2. PRECAUTIONS

· In the **GENERAL** subsection, the last paragraph was revised as follows:

"As with other quinolones, disturbances of blood glucose, including symptomatic hyper- and hypoglycemia, have been reported with TEQUIN, usually in diabetic patients receiving concomitant treatment with oral hypoglycemic agents (e.g., glyburide) ~~or~~ with or without insulin. In these patients, the careful monitoring of blood glucose is recommended. If a hypoglycemic reaction occurs in a patient being treated with TEQUIN, appropriate therapy should be initiated immediately and TEQUIN should be discontinued. (See **CLINICAL PHARMACOLOGY, PRECAUTIONS: Drug Interactions**, and **ADVERSE REACTIONS.)**

· In the **Information for Patients** subsection, the twelfth bullet was revised as follows:

~~"•that if they are diabetic and are being treated with insulin or an oral hypoglycemic agent and a hypoglycemic reaction occurs, they should discontinue gatifloxacin and consult a physician (see **PRECAUTIONS: General**)."~~

"•that if they are diabetic, disturbances of blood glucose, including symptomatic hyper- and hypoglycemia, have been reported in patients treated concomitantly with TEQUIN (as with other quinolones) and oral hypoglycemic agents with or without insulin. If a hypoglycemic reaction occurs, they should initiate appropriate therapy immediately, discontinue TEQUIN, and contact a physician (see **PRECAUTIONS: General** and **Drug Interactions**)."

· In the **Drug Interactions** subsection, a paragraph concerning **Antidiabetic agents** has been added and appears second in this subsection as follows:

"**Antidiabetic agents:** No significant pharmacokinetic interactions have been observed when glyburide was administered concomitantly with TEQUIN. However, disturbances of blood glucose, including symptomatic hyper- and hypoglycemia, have been reported in patients treated concomitantly with TEQUIN (as with other quinolones) and oral hypoglycemic agents with or without insulin. Therefore, careful monitoring of blood glucose is recommended when TEQUIN is administered to diabetic patients receiving treatment with oral hypoglycemic agents with or without insulin. (See **CLINICAL PHARMACOLOGY** and **PRECAUTIONS: General** and **Information for Patients.**)"

3. ADVERSE REACTIONS

· The fifth and sixth paragraphs were revised to include additional adverse events as follows:

Body as a Whole: allergic reaction, asthenia, back pain, chest pain, chills, face edema, fever, halitosis
Cardiovascular System: hypertension, palpitation
Digestive System: abdominal pain, anorexia, constipation, dyspepsia, flatulence, gastritis, glossitis, mouth ulcer, oral moniliasis, stomatitis, vomiting
Hemic/Lymphatic System: ecchymosis
Metabolic/Nutritional System: hyperglycemia, peripheral edema, thirst
Musculoskeletal System: arthralgia, leg cramp
Nervous System: abnormal dream, agitation, anxiety, confusion, hallucination, insomnia, nervousness, paresthesia, somnolence, tremor, vasodilatation, vertigo
Respiratory System: dyspnea, pharyngitis
Skin/Appendages: dry skin, pruritus, rash, sweating
Special Senses: abnormal vision, eye pain, taste perversion, tinnitus
Urogenital System: dysuria, hematuria

Additional drug-related adverse events considered clinically relevant that occurred in <0.1% (rare adverse events) of patients receiving gatifloxacin in single- and multiple-dose clinical trials are as follows: abnormal thinking, ~~agitation,~~ alcohol intolerance, ~~anorexia, anxiety, arthalgia~~, arthritis, ~~asthenia,~~ asthma (bronchospasm), ataxia, bone pain, bradycardia, breast pain, cheilitis, colitis, ~~confusion~~, convulsion, cyanosis, depersonalization, depression, diabetes mellitus, ~~dry skin~~, dysphagia, ear pain, ~~ecchymosis~~, edema, epistaxis, euphoria, ~~eye pain, face edema, flatulence, gastritis,~~ gastrointestinal hemorrhage, gingivitis, ~~halitosis, hallucination~~, hematemesis, hostility, hyperesthesia, ~~hyperglycemia, hypertension,~~ hypertonia, hyperventilation, hypoglycemia, ~~leg cramp~~, lymphadenopathy, maculopapular rash, metrorrhagia, migraine, mouth edema, myalgia, myasthenia, neck pain, ~~nervousness,~~ panic attack, paranoia, parosmia, ~~pruritus~~, pseudomembranous colitis, psychosis, ptosis, rectal hemorrhage, ~~somnolence,~~ stress, substernal chest pain, tachycardia, taste loss, ~~thirst,~~ tongue edema, vesiculobullous rash.

4. HOW SUPPLIED

• The **Tablets** subsection was revised to add information concerning the blister pack of 7 tablets (TEQUIN Teq-Paq™).

5. Patient Information About Tequin®

• In the section called "**What about other medications I am taking?"** the following bullet was added and now appears third as follows:

"• If you have diabetes, it is important to let your healthcare provider know if you are on oral hypoglycemic agents with or without insulin."

• In the section called **"What are the possible side effects of TEQUIN?"** a paragraph was added to the end of this section as follows:

> "If you have diabetes, you should know that disturbances of blood sugar, including symptoms of hyperglycemia (high blood sugar) and hypoglycemia (low blood sugar), have been reported in patients treated concomitantly with TEQUIN (as with other quinolone antibiotics) and oral antidiabetic drugs with or without insulin. If you develop symptoms of low blood sugar while on TEQUIN, you should take immediate measures to increase your blood sugar, stop taking TEQUIN, and contact your healthcare professional at once."

6. Several miscellaneous typographical errors were corrected throughout the label and "gatifloxacin" was added in parentheses each time "Tequin®" was mentioned.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the submitted final printed labeling (package insert submitted April 17, 2001). Accordingly, these supplemental applications are approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Robin Anderson, Labeling Reviewer, at (301) 827-2127.

Sincerely,

Mark J. Goldberger, M.D. M.P.H.
Director
Division of Special Pathogen and Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research